JTCM 中医杂志

Online Submissions: http://www.journaltcm.com
info@journaltcm.com

J Tradit Chin Med 2013 February 15; 33(1): 1-8
ISSN 0255-2922

SYSTEMATIC REVIEW

Effect of Jianpi therapy in treatment of chronic obstructive pulmonary disease: a systematic review

Zhen Gao, Yingying Liu, Juhong Zhang, Halmurat·Upur

Zhen Gao, Traditional Chinese Medicine Hospital Affiliated to Xinjiang Medical University & National Clinical Research Base of Traditional Chinese Medicine, Ulumuqi 830000, Xinjiang, China

Zhen Gao, Yingying Liu, Juhong Zhang, Halmurat·Upur, Xinjiang Medical University, Ulumuqi 830011, Xinjiang, China

Supported by Program for Changjiang Scholars and Innovative Research Team in University, Ministry of Education of China (NO. IRT0977)

Correspondence to: Prof. Halmurat·Upur, Xinjiang Medical University, Ulumuqi 830011, Xinjiang, China. halmurat@263.net

Telephone: +86-13609923639

Accepted: March 3, 2012

Abstract

OBJECTIVE: To evaluate the efficacy of Jianpi therapy in Traditional Chinese Medicine (TCM) for treatment of chronic obstructive pulmonary disease (COPD) in stable phase by performing a systematic review and meta-analysis.

METHODS: The literatures concerning randomized controlled trials (RCTs) and quasi-RCTs comparing TCM treatment plus Western Medicine (WM) treatment with TCM alone, or TCM treatment vs no treatment, placebo for stable phase of COPD were searched in PubMed (1990-December 2010), in English and using Chinese National Knowledge Infrastructure (CNKI, 1990-December 2010), Chinese Biomedical Database (1990-December 2010), Wangfang Database (1990-December 2010), and Weipu (VIP) Database in Chinese. The quality assessment and data extraction for RCTs were conducted by two reviewers independently. Jadad scale and allocation concealment were used to assess the quality of the included studies, and meta-analyses were conducted with the Collaboration's Revman 5.0 software.

RESULTS: Seventeen RCTs or quasi-RCTs involving 1269 patients were included. The methodological quality was poor in all trials except one trial (Jadad score=4). In the meta-analysis, TCM-WM treatment was significantly superior to WM treatment in cure rate [*OR*=3.82, 95%*CI* (2.45, 5.95)], and the effective rate between TCM treatment and placebo also had significant difference [*OR*=4.31, 95%*CI* (2.35, 7.91)]. Moreover, pulmonary function of the patients in TCM-WM group and TCM group was significantly improved [forced vital capacity (FVC), *P*=0.01, quality of life, *P*<0.001].

CONCLUSION: The experience in TCM-WM treatment of COPD in stable phase was encouraging. The current evidence shows that TCM-WM treatment might be more efficient in effective rate, quality of life, and FVC than WM treatment alone. But for forced expiratory volume in one second (FEV1) and FEV1/FVC, no matter TCM-WM treatment compared with WM treatment alone or TCM treatment compared with placebo, there was no significant difference, with no obvious adverse reactions. Due to the low methodological quality of trials included, more RCTs of high quality in large scale are required.

Key words: Pulmonary disease, chronic obstructive; Meta-analysis; Traditional Chinese Medicine; Randomized controlled trial; Jianpi therapy

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), characterized by progressive expiratory aiflow limitation, is a major cause of chronic morbidity and mortality worldwide.[1] According to the World Health Organization (WHO),[2] the total number of deaths from COPD in the world are projected to increase by 30% in the next 10 years; by 2030, COPD would become the fourth leading cause of death worldwide. Among all the major chronic diseases, COPD is the only disease that shows a rising mortality. These increases are mainly linked to the epidemic of tobacco exposure and the indoor and outdoor air pollution in Asian countries.

The goals of treatment for COPD are to control acute attack and improve pulmonary function, prevent serious long-term consequences of pulmonary heart disease and respiratory failure. Treatment for patients in stable phase is very important to the fate of COPD. In China, Traditional Chinese Medicine (TCM), as an auxiliary therapy to Western Medicine (WM), was extensively employed for the treatment of stable COPD. In our clinic, it was found that patients with COPD had damage to the spleen functions. Accordingly, Jianpi prescription was chosen as it strengthens body resistance through strengthening the spleen. So, Jianpi therapy became one of the main methods in TCM for stable COPD. In parallel with the Jianpi therapy, a series of studies were conducted to evaluate the effectiveness of Jianpi auxiliary therapy in WM, Jianpi therapy versus WM alone and placebo. To date, some of the randomized controlled trials have investigated the beneficial effects of Jianpi auxiliary therapy in WM and the Jianpi therapy alone in improvement of the clinical symptoms, and the pulmonary function in stable COPD. However, the results were inconsistent due to different in study design and outcome measures. So, we conducted a meta-analysis using updated literature searches to asses the effects and to determine whether Jianpi auxiliary therapy in WM or Jianpi therapy alone were more efficacious than WM alone/placebo in improving the clinical symptoms, increasing lung function, increasing quality of life, and improving the other clinical outcomes.

METHODS

Truly or quasi-randomized controlled trials (RCTs) of TCM for COPD were included, regardless of whether the intervention was blinded to the patients, clinicians or researchers after randomization was done. Trials compared WM with TCM in the control arm were also included. Trials using animals or their processed products were excluded. All eligible literature was included regardless of language. In accordance with our main purpose outlined above, the trials that used TCM in both the treatment and control groups were excluded, as well as the trials that did not report diagnostic criteria. Figure 1 shows the flowchart of the present systematic review.

Literature search

Literature search was performed using PubMed (1990-December 2010), in English by 2 reviewers (Juhong Zhang and Zhen Gao) and using Chinese National Knowledge Infrastructure (CNKI) (1990-December 2010), Chinese Biomedical Database (1990-December 2010), Wangfang Database (1990-December 2010), and VIP Database in Chinese by 2 reviewers (Juhong Zhang and Zhen Gao). Key words used in the search were Chronic Obstructive Lung Disease, COPD, Jianpi (means invigorating the spleen, strengthening the spleen, or nourishing the spleen). Various combinations of the search terms were used depending on the database searched. The type of publication searched was clinical study. Two reviewers for the English literature and Chinese literature worked independently for inclusion. Any disagreements were resolved through discussion.

Data extraction

For the included studies, data were extracted by 2 reviewers (Juhong Zhang and Zhen Gao). Once completed, any disagreements on data extraction and study evaluation were resolved through discussion. The data included study design, patient characteristics, and medication use.

Data analysis

Data were analyzed using Revman 5.0 downloaded from the website of Cochrane collaboration. Meta-analysis was performed for the data. The dichotomous data were expressed as odds ratio (*OR*) with corresponding 95% confidence interval (95% *CI*). For continuous data, standardized mean difference (*SMD*) and 95% *CI* were calculated. Heterogeneity was tested by χ^2 test. The comparison (Figure 2-4) was split into two parts: first comparing TCM with WM, and second comparing TCM plus WM to WM alone. Although the constituents of the compounds were different in each investigation, the whole compounds of TCM should have the following benefits of nourishing *Qi* and kidney, strengthening spleen and lung. A process was designed to combine across studies to perform a meta-analysis. If the main effects of the whole compound in the studies were similar, the data was combined. The fixed-effect mode was used to combine dichotomous data if homogeneity was found. If heterogeneity was found, the random effect mode was alternatively used. To make the meta-analysis more clinically meaningful, publication bias would be examined by the funnel plot.

RESULTS

Identified studies and characteristics

The English- and Chinese-language literature search

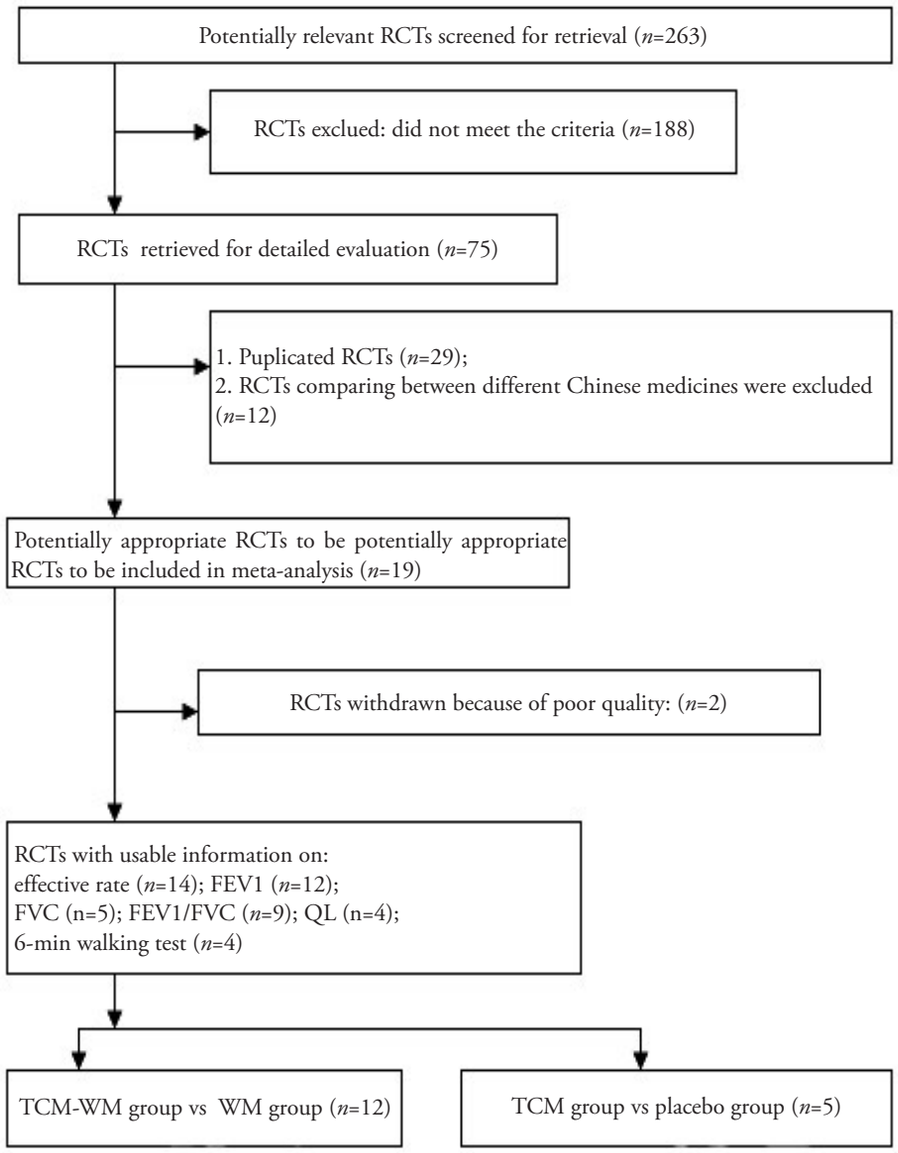

Figure 1 Flow chart with literature search results

RCT: randomized controlled trial; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; QL: quality of life; TCM: Traditional Chinese Medicine; WM: Western Medicine.

yielded a total of 263 published studies, of which the abstracts were reviewed, and then 188 studies were excluded because lack of the controls. The 75 RCTs that were potentially relevant were further reviewed, of which 56 were excluded, 29 because of the duplicate publications, 12 because of comparing between different Chinese medicines, 15 because of pseudorandom and nonrandomized. Finally, 19 RCTs or quasi-RCTs that met the inclusion criteria were included. A total of 1587 subjects in 19 RCTs with a diagnosis of stable COPD were included (Table 1). However, only 1496 subjects in 17 RCTs were included in Meta analysis (2 RCTs were excluded because of poor quality, but included in the systematic review) (Figure 1).

Quality assessment

Table 2 shows the methodologic qualities of trials. Of the 19 RCTs,[3-21] most of them did not provide adequate information about the methods of blinding, and none of them provide adequate information about ITT. According to the Jadad scoring method, of the 19 RCTs, 1 study[16] scored 4 points, 4 studies[6-8,18] scored 3 points, 5 studies scored 2 points,[4,5,13,17,21] and the remaining 9 studies[3,9-15,19,20] each scored 1 point. According to the Allocation concealment, 4 RCTs[8,16,18,21] got B, 14 RCTs [3-7,10-15,17,19,20] got C, and 1[9]got D (poor quality).

Meta-analysis

In meta-analysis, we only analysed the ending indexes which had no significant heterogeneity. 12 studies compared TCM with WM were included in meta-analysis. Since they nourished the spleen, we combined data across 12 studies. Notably, the meta-analysis of high-quality trials demonstrated that there was significant difference in cure rate between TCM-WM group and WM group [total *OR*=3.59, 95% *CI* (2.33, 5.52)] without heterogeneity (χ^2=5.52, *df* =8). The significant difference was also found in cure rate between TCM group and placebo group [total *OR*=2.81, 95% *CI* (1.41, 5.59)] without heterogeneity (χ^2=1.66, *df*=2)

Table 1 The characteristics of trials

Trail	Participants	Range of age (year)	Duration (week)	Intervention measure		Ending index
	T/C	T/C		Treatment	Control	
TCM-WM vs WM						
Feng XZ 2006[15]	36/33	unclear	30	Oral aminophylline +Jianpi and Bufei	Oral aminophylline	①②③
Liu DP 2007[14]	32/30	62/53	12	Oral compound ipratropium bromide+Bushen, Jianpi and Huayu	Oral compound ipratropium bromide	①②③
Wang S 2005[13]	20/20	59±8/61±8	8	Oral ambroxol hydrochloride+inhal salbutamol+Yifei and Jianpi	Oral ambroxol hydrochloride+ inhal salbutamol	②③
Wang JR 2010[12]	45/45	69/68	12	Inhal salbutamol+Jianpi	Inhal salbutamol	①
Sun Sh 2010[11]	38/38	55±11/55±11	12	Oral theophylline+inhal salbutamol + Jianpi Hutan	Oral theophylline+ inhal salbutamol	①②③⑥
Shan LY 2007[10]	28/27	67±6/67±5	24	Oral theophylline+Jianpi	Oral theophylline	①
Song C 2009[3]	30/30	66±8/64±10	4	Inhal salbutamoloral +oral Bufei, Jianpi and Yishen	Inhal salbutamoloral	①②③④⑤
Han H 2009[4]	29/29	69±5/69±7	12	Oral theophylline+oral Jianpi and Yifei	Oral theophylline	①②③⑥
Liang AL 2009[5]	30/30	71±8/71±9	12	Oral salmeterol+ aminophylline +oral Jianpi and Yifei	Oral salmeterol+ aminophyl line	①②③⑤
Fu ZY 2008[6]	30/30	70±5/68±6	Unclear	Oral Jianpi and Yifei+ ambroxol hydrochloride	Ambroxol hydrochloride	①②④⑥
Lin XL 2010[8]	30/30	71±6/70±6	12	oral Jianpi Yifei+Ambroxol Hydrochloride	Ambroxol Hydrochloride	①⑥
Qi WP 2009[7]	30/30	70±7/74±7	8	Oral aminophylline +Yiqi and Jianpi	Oral aminophylline	②⑤
Wu YQ 2007[a9]	63/59	62/62	12	Oral erythromycin+Yiqi and Jianpi	Oral erythromycin	②③⑥
TCM vs placebo						
Ke XX 2010[16]	131/60	69±8/68±8	8	Oral Jianpi and Yifei	Placebo	②③⑤
Li YL 2007[17]	30/30	69±8/71±6	8	Oral Gubenshengjin	Blank	①②③④⑥
Lin L 2003[18]	30/30	62/60	8	Oral Jianpi and Yifei	Blank	①②⑥
Zhang MX 2006[19]	24/22	67±7/68±5	24	Oral Jianpi and Yifei	Blank	①②③④
Tang CY 2004[20]	30/30	70/70	8	Oral Jianpi and Yifei	Placebo	①④
Liu H 2006[21]	120/60	67±10/66±10	8	Gushen Dingchuan	Blank	②③⑥

Notes: T: treatment; C: control; TCM: Traditional Chinese Medicine; WM: Western Medicine; T/C: treatment/control. ① total effective rate, ② FEV1: forced expiratory volume in one second;③ FEV1/FVC: forced expiratory volume in one second/ forced vital capacity; ④ QL: quality of life; ⑤ 6-MWT :6-minute walking test; ⑥ FVC :forced vital capacity. [a]Not included in meta-analysis.

(Figure 2).

We also analyzed the pulmonary function and quality of life (QL) in RCTs. Three studies compared the FVC between TCM-WM group and WM group [*SMD*= 0.36, 95% *CI* (0.08, 0.36), *P*=0.01] without heterogeneity (χ^2=1.57, *df*=2), and two studies compared the QL between the two groups [*SMD*=-0.82, 95% *CI* (-1.21, -0.43), *P*<0.0001] (Figure 3).

Between TCM group and placebo group, only FVC was significantly improved in TCM group [total *SMD*= 0.54, 95% *CI* (0.27, 0.81), *P*<0.0001]. However, no significant difference was found in other parameters of pulmonary function (FEV1and FEV1/FVC) between the two groups (*P*>0.05) (Figure 4).

Because of significant heterogeneity, some parameters of the trials were not included in meta-analysis. Table 3 shows the outcome end-points which were not included in meta-analysis but reported in RCTs.

The funnel plot (Figure 5) shows that there was significant publication bias in effective rate. With fewer than five trials to compare, we did not examine publication bias of the other ending indexes in meta-analysis.

DISCUSSION

To date, using the bronchodilator and inhaled steroids for patients with COPD remains controversial. Bronchodilator has a modest effect on improving lung function. Steroids inhaled are given only for the patients with more severe airway obstruction and frequent exac-

Table 2 The methodological quality of trials

Trial	Follow-up duration (month)	Jadad score	Allocation concealment
TCM-WM vs WM			
Feng XZ 2006[15]	Unclear	1	C
Liu DP 2007[14]	Unclear	1	C
Wang S 2005[13]	Unclear	2	C
Wang JR 2010[12]	12	1	C
Sun SH 2010[11]	3	1	C
Shan LY 2007[10]	Unclear	1	C
Sun C 2009[3]	Unclear	1	C
Han H 2009[4]	Unclear	2	C
Liang AL 2009[5]	3	2	C
Fu ZY 2008[6]	Unclear	3	C
Lin XL 2010[8]	Unclear	3	B
Qi WP 2009[7]	Unclear	3	C
Wu YQ 2007[9]	Unclear	1	D
TCM vs placebo			
Ke XX 2010[16]	4	4	B
Li YL 2007[17]	Unclear	2	C
Li L 2003[18]	Unclear	3	B
Zhang MX 2006[19]	Unclear	1	C
Tang CY 2004[20]	Unclear	1	C
Li H 2006[21]	Unclear	2	B

erbations.[1] Treatment with the combined use of inhaled steroids and long-acting bronchodilators improves the lung function, clinical symptoms and quality of life as compared with the placebo treatment, but the reports on its effects compared with its mono-components are conflicting.[22,23] The combination therapy reduces sputum neutrophil percentage, sputum eosinophil counts, and biopsy CD8 lymphocytes in stable COPD.[24] Despite the modest beneficial effects, withdrawal of inhaled steroids may result in deterioration to lung function. So, TCM is an ideal therapeutic method to make up this shortcoming. Many trials show that TCM can improve patients' pulmonary function and quality of life.

In the present study, we summarized the results of the findings from 17 RCTs using meta-analysis; 2 RCTs were included in the systematic review, but they were excluded from meta-analysis because of poor quality. There is no convincing evidence to support that Jianpi auxiliary therapy as well as WM/Jianpi therapy could significantly improve effective rate and pulmonary function. However, the treatment of COPD with a combination of Chinese and Western medicine could improve effective rate, pulmonary function and quality of life, as compared with the findings from Zhou et al's study.[25]

The traditional Western Medicine treatment of COPD are using bronchodilators and anti-inflammatory. Generally, we should not consider that in the treatment of COPD, WM is effective or not. And we can evaluate the short-term or long-term efficacy of bronchodilator asthma medications or anti-inflammatory treatment for COPD. One systematic review about TCM treatment of COPD in stable phase has been reported,[25] but the treatment is TCM not the Jianpi therapy only. If we don't make this systematic review, those who don't know much about TCM may say TCM is a method that may be useful for COPD. But TCM is not a method, just like WM, it include many different methods, some methods may be useful for COPD, and some may not. So, if you put all the methods together to do the evaluation, it may be hard to evaluate the effect of TCM.

In TCM, Lung belongs to "metal", and Spleen belongs to "soil". TCM holds that "soil can transform into metal". That is to say, "soil (spleen)" is the mother of "metal (lung)", and the "mother organ (spleen)" can supply some essence to "son organ (lung)", just like the land can provide nutrients to plants. If the "son organ (lung) " is becoming weak, it will overuse the essence that the "mother organ (spleen)" supply; and in order to meet the "son organ (lung)"'s need, the "mother organ (spleen)" will sooner or later become weak too, then it can not give enough essence, so the "son organ (lung)" will become weaker and weaker. It is also considered in TCM that the spleen is the basis of acquired constitution. Above all, Jianpi therapy is one of the important methods of TCM for treating chronic lung diseases, but whether Jianpi therapy is useful or not for treating COPD in sable phase is still lack of systematic evaluation. Therefore, we conducted this systematic review to evaluate Jianpi therapy of TCM for treating COPD in stable phase.

In this study, the analyses provided clear evidence to support the notion that the TCM-WM treatments might be more efficient in effective rate, quality of life, FVC, than WM treatment alone. But for FEV1 and FEV1/FVC, no matter TCM-WM treatment compared with WM treatment alone or TCM treatments compared with placebo, there was no significant difference. The present results were partly consistent with the results from a previously published meta-analysis.[25]

Our results suggest that the adjunctive treatment of TCM could significantly improve the patients' quality of life, but this maybe just change the patients' feeling, not really improve the patients' pulmonary function. Quality of life was improved significantly in TCM-WM group (P<0.0001), but no significant difference was found in other parameters of pulmonary function (FEV1 and FEV1/FVC) between the two groups (P>0.05). There was no doubt that TCM can significantly improve effective rate, how well such effects could be translated into clinical outcomes were unknown. This aspect of benefits warrants further investigation.

The results of this study should be considered within

Table 3 The outcome end-points which were not included in mata-analysis reported in RCTs

Trial	Intervention measure		Significance of Ending indexes (*P*)[a]		
	Treatment	Control	FEV1	FEV1/FVC	6-MWT
TCM-WM vs WM					
Feng XZ 2006[15]	Oral aminophylline +Jianpi and Bufei	Oral aminophylline	<0.05	<0.05	-
Liu DP 2007[14]	Oral compound ipratropium bromide+Bushen, Jianpi and Huayu	Oral compound ipratropium bromide	>0.05	>0.05	-
Wang S 2005[13]	Oral ambroxol hydrochloride+ inhal salbutamol+Yifei and Jianpi	Oral ambroxol hydrochloride+inhal salbutamol	>0.05	>0.05	-
Wang JR 2010[12]	Inhal salbutamol+Jianpi	Inhal salbutamol	-	-	-
Sun SH 2010[11]	Oral theophylline+inhal salbutamol + Jianpi and Huatan	Oral theophylline+ inhal salbutamol	-	-	-
Shan LY 2007[10]	Oral theophylline+Jianpi	Oral theophylline	-	-	-
Song C 2009[3]	Inhal salbutamoloral +oral Bufei, Jianpi and Yishen	Inhal salbutamoloral	-	-	<0.05
Han H 2009[4]	Oral theophylline+oral Jianpi and Yifei	Oral theophylline	<0.05	>0.05	-
Liang AL 2009[5]	Oral salmeterol+aminophylline +oral Jianpi and Yifei	Oral salmetero l+ aminophylline	>0.05	>0.05	<0.05
Fu ZY 2008[6]	Oral Jianpi and Yifei+ambroxol hydrochloride	ambroxol hydrochloride	>0.05	-	-
Lin XL 2010[8]	Oral Jianpi and Yifei+ambroxol hydrochloride	Ambroxol hydrochloride	-	-	<0.05
Qi WP 2009[7]	Oral aminophylline +Yiqi and Jianpi	Oral aminophylline	>0.05	-	-
TCM vs Placebo					
Ke XX 2010[16]	Oral Jianpi and Yifei	Placebo	>0.05	-	<0.05
Li YL 2007[17]	Oral Gubenshengjin	Blank	>0.05	>0.05	-
Liu H 2006[21]	Gushen Dingchuan	Blank	<0.05	-	-
Zhang MX 2006[19]	Oral Jianpi and Yifei	Blank	<0.05	>0.05	-
Tang CY 2004[20]	Oral Jianpi and Yifei	Placebo	-	>0.05	-

Notes FEV1: forced expiratory volume in one second; FVC: forced vital capacity; 6-MWT: 6-min walking test; TCM: Traditional Chinese Medicine; WM: Western Medicine. [a]Compared in parameters of pre-and post-treatment between the groups.

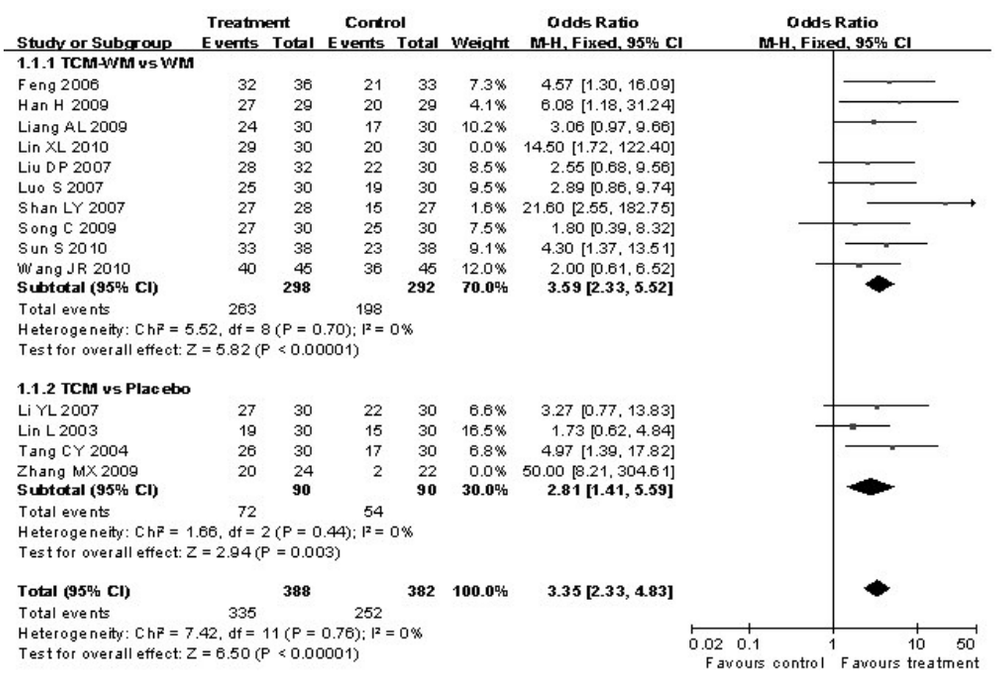

Figure 2 Meta-analysis for comparison of effective rate between TCM-WM group and WM group
TCM: Traditional Chinese Medicine; WM: Western Medicine

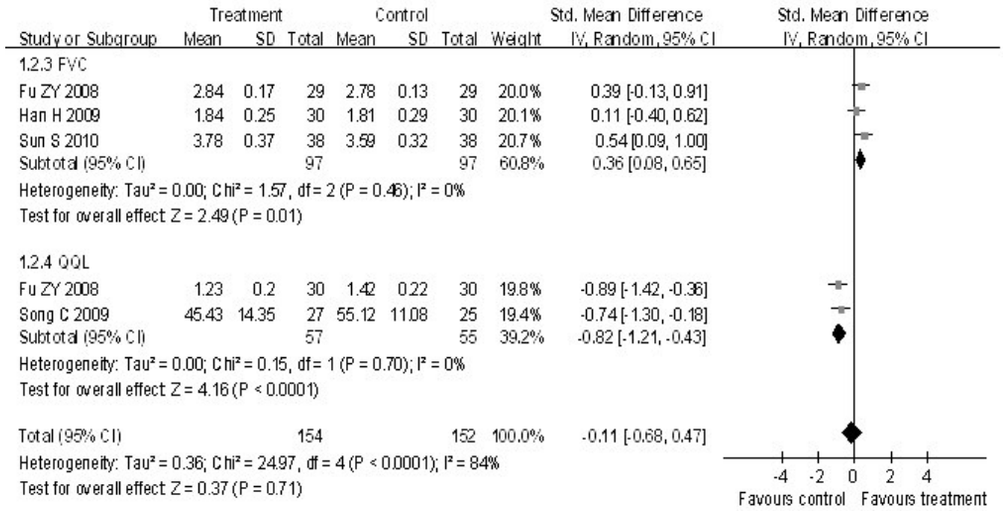

Figure 3 Meta-analysis for comparison of pulmonary function and QL parameters between TCM-WM group and WM group
QL: quality of life; TCM: Traditional Chinese Medicine; WM: Western Medicine

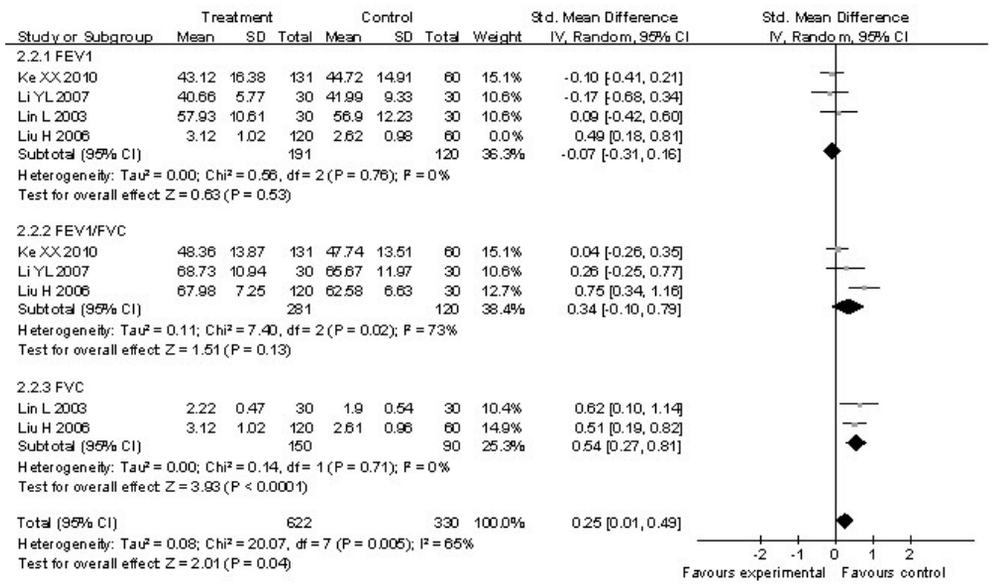

Figure 4 Meta-analysis for comparison of pulmonary function parameters between TCM group and placebo group
TCM: Traditional Chinese Medicine.

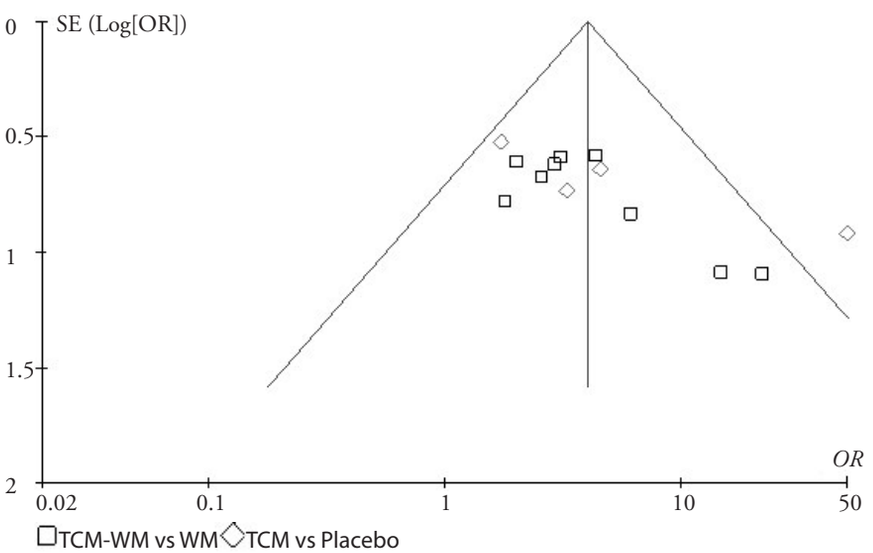

Figure 5 Funnel plot of effective rate
TCM: Traditional Chinese Medicine; WM: Western Medicine.

the context of limitations. First, most of the 17 clinical studies had low methodological quality according to the Jadad scores. Second, there were only 2 studies that reported the full three basic index of pulmonary func-

tion, and no RCT report the outcomes of high-resolution RCT. Third, the variation in treatment regimens, particularly the wide range of TCM in dose, certain herbs, route of administration, and duration of therapy, became a major obstacle to a clear interpretation of the results. Last, we examine the publication bias with a funnel plot, publication bias may exist in trials.

The experience in TCM-WM treatment of COPD in stable phase was encouraging. The current evidence shows that the integrated traditional and Western Medicine tends to relieve the symptoms and improve quality of life for patients with stable COPD without obvious adverse reactions. Due to the low methodological quality of trials included, more RCTs of high quality in large scale are required.

REFERENCES

1 **Fabbri** LM, Hurd SS. Global Strategy for the Diagnosis, Management and Prevention of COPD: 2003 update. Eur Respir J 2003; 22(1): 1-2.

2 World Health Organization. World health report 2002: reducing risks, promoting healthy life. Available from URL: www.who.int/whr/2002. Accessed December 21, 2007.

3 **Song C**. Clinical observation on BufeiJianpiYishen decoction for treatment of COPD and mechanism study on regulating TlymPhocyte immunologic function. Chengdu Zhong Yi Yao Da Xue 2009; 21-30.

4 **Han H**. The Research on Curative Effect and Influence of Transforming Growth Factor-β1 of Chronic obstructive Pulmonary Disease with Deficiency of both the Lung and Spleen in Stab1e Phase by Feikangkeli. Guangzhou Zhong Yi Yao Da Xue 2009; 20-25.

5 **Liang AL**. The Effect of spleen-transporting kidney-boosting lung-supplementing methods in improving stable phase of COPD patients life quality. Beijing Zhong Yi Yao Da Xue 2009; 43-59.

6 **Fu ZY**. Study on efficacy of COPD with the invigorating spleen, Eliminating phlegm and activating blood circulation therapy, and its effect on pulmonary function, quality of life. Guangzhou Zhong Yi Yao Da Xue 2008; 21-27.

7 **Qi WP**. Effect of supplementing *Qi* to invigorate the spleen herbs on exercise endurance in patients with stable chronic obstructive pulmonary disease. Zhejiang Zhong Yi Yao Da Xue 2009; 2-5.

8 **Lin XL**. The research on curative effect and influence of respiratory muscle fatigue of chronic obstructive pulmonary disease with deficiency of both lung and spleen in stable phase by tonifying lung and spleen. Guangzhou Zhong Yi Yao Da Xue 2010; 30-35.

9 **Wu YQ**, Huang ZA. An observation of Macrolides plus Liujunzitang for COPD in stable phase. Hua Xia Yi Xue 2007; 20(6): 1213-1215.

10 **Shan LY**, Liu XH, Zhong LH. A clinical observation on the effect of Peitu shengjin method for chronic obstructive pulmonary disease in stable phase. Hubei Zhong Yi Za Zhi 2007; 29(4): 26-27.

11 **Sun S**. Clinical observation on chronic obstructive pulmonary disease treated with method of invigorating spleen to remove phlegm. Zhong Guo Zhong Yi Ji Chu Yi Xue Za Zhi 2010; 16(2): 143-144.

12 **Wang JR**. Clinical study in 45 cases of chronic obstructive pulmonary disease treated with Jianpi Yifei method. Zhong Guo Shi Yong Yi Yao 2010; 5(10): 143.

13 **Wang S**, Ji HY, Zhang NZ, et al. Effect of Jianpi recipe on inflammatory cells, levels of interleukin-8 and tumor necrosis factor-α in sputum from patients with chronic obstructive pulmonary disease. Zhong Guo Zhong Xi Yi Jie He Za Zhi 2005; 25(2): 111-113.

14 **Liu DP**, Hong HJ. A Clinical observation on the effect of Jianpi Huayu for chronic obstructive pulmonary disease in stable phase. Zhong Guo Zhong Yi Ji Zheng 2007; 16(2): 152, 197.

15 **Feng XZ**, Yao HQ. Clinical study in 36 cases of chronic obstructive pulmonary disease in stable phase treated with Jianpi Bufei plus Western Medicine. Qinghai Yi Yao Za Zhi 2006; 36(9): 82-83.

16 **Ke XX**. Study on clinical application of lung-spleen correlation theory in the stable phase of chronic obstructive pulmonary disease. Guangzhou Zhong Yi Yao Da Xue 2010; 9-40.

17 **Li YL.** The effect of the measure of strengthening spleen and nourishing kidney for treating malnutrition caused by COPD disease. Guangzhou Zhong Yi Yao Da Xue 2007; 11-19.

18 **Lin L**, Tang CY, Xu YJ. Clinical observation of "spleen-lung nourishing granule" in treating respiratory muscle fatigue of stable chronic obstructive pulmonary disease. Shanghai Zhong Yi Za Zhi 2003; 37(11): 10-12.

19 **Zhang MX**. A clinical observation of spleen-lung nourishing and kidney-boosting granule for chronic obstructive pulmonary disease in stable phase. Zhong Guo Zhong Yi Yao Xin Xi Za Zhi 2006; 13(7): 64-65.

20 **Tang CY**, Lin L, Xu YJ. The clinical research into the effect of the backing up earth to generate metal on life quality in COPD patients in stable phase. Fujian Zhong Yi Yao 2004; 35(5): 1-4.

21 **Liu H**, Cheng YF, Li QY, Gao TL. The effects of Wenshen Naqi,Jianpi Lishui on lung function for chronic obstructive pulmonary disease in stable phase patients. Zhong Guo Zhong Yi Ji Zheng 2006; 15(2): 116-117.

22 **Nannini LJ**, Cates CJ, Lasserson TJ, Poole P. Combined use of corticosteroid and long acting beta-agonist in one inhaler for chronic obstructive pulmonary disease. Cochrane Database Syst Rev Published Online: 20 JAN 2010, Assessed as up-to-date: 1 AUG 2007. Available from URL: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003794.pub3/full.

23 **Calverley PMA**, Anderson JA, Celli B, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. N Engl J Med 2007; 356(8): 775-789.

24 **Barnes NC**, Qiu YS, Pavord ID, et al. Antiinflammatory effects of salmeterol/fluticasone propionate in chronic obstructive lung disease. Am J Respir Crit Care Med 2006; 173(7): 736-743.

25 **Zhou W**, Zhong YQ, Yang HM, et al. Traditional Chinese Medicine in the treatment of chronic obstructive pulmonary disease in stable stage: a systematic review of randomized controlled trials. Zhong Guo Xun Zheng Yi Xue Za Zhi 2009; 9(3): 311-318.